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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/325,095	06/03/1999	IAN D. HILES	LUD5246.4JEL	2392
24972	7590	11/12/2004	EXAMINER	
FULBRIGHT & JAWORSKI, LLP 666 FIFTH AVE NEW YORK, NY 10103-3198			HINES, JANA A	
			ART UNIT	PAPER NUMBER
			1645	

DATE MAILED: 11/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b>	<b>Application No.</b> 09/325,095	<b>Applicant(s)</b> HILES ET AL.	
	<b>Examiner</b> Ja-Na Hines	<b>Art Unit</b> 1645	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 22 June 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☐ The period for reply expires \_\_months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 27 July 2004. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: None.

Claim(s) objected to: None.

Claim(s) rejected: 51-58, 60 and 61.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.

10. ☐ Other: \_\_\_\_\_

  
**LYNETTE R. F. SMITH**  
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Continuation of 5. does NOT place the application in condition for allowance because: The written description rejection of claims 51-58 and 60-61 under 35 U.S.C. 112, first paragraph, is maintained. The rejection was on the grounds that specification and claims lack sufficient written description of a method for determining expression of a gene that encodes a human polypeptide comprising a contact step wherein the determination of hybridization determines the expression of said gene. Applicants' assert that they do not understand why/how the hybridization and PCR methods do not describe a method for determining gene. The hybridization process allows two complementary nucleic acid strands to form a double helix during an annealing period. The process can also screen for the presence of a particular gene. Thus hybridization techniques will not determine gene expression. PCR teaches ways to amplify a specific DNA segment. Thus PCR alone or in combination with hybridization techniques will not determine gene expression. Rather, the best the techniques can do is determine the presence of a sequence and amplify it, not determine its expression. Therefore the rejection is stating that the determination of gene expression will not result from contacting a sample with a nucleic acid molecule which hybridizes to a transcript of the gene. Applicants' point to examples drawn to Northern and Southern Transfer techniques. However Northern techniques describe encoding RNA's with a DNA probe and allowing hybridization to occur. Southern Blotting techniques use double stranded DNA molecules to determine hybridization. There is no teaching that the resulting hybridization will determine gene expression. There is no disclosure of how the annealing process will determine the expression of a gene. These techniques may describe determining the presence of a gene, but they do not determine gene expression. Therefore the hybridization assays described on pages 44, 46-47 and 52-53 fail to disclose a method for determining gene expression. There is no scientific correlation supported by the specification that if hybridization occurs, gene expression will occur. The monitoring for protein expression of transcripts can be achieved using techniques such as immunological techniques, pulse-chase labelling, immunoprecipitation, epitope tagging, immunohistochemistry and surrogate reporter protein detection. However the specification fails to describe methods for determining gene expression. Therefore, contrary to applicants' assertions, there is no description of a method for determining the expression of a gene and applicants' arguments are not persuasive. There still appears to be no support in the specification for contacting a sample with a nucleic acid molecule that hybridizes to a transcript of the gene and determines that hybridization and equates to the determination of gene expression in the claimed manner. Applicants' have failed to point to support in their response. Applicants' argue that RNA works in the sample because of the statement that the sample has to be RNA, since DNA cannot discriminate the transcript of said gene. Normally, mRNA leads to cDNA which leads to amplification. The fact that RNA works in the sample is agreed upon. However the issue is about DNA, not RNA. And applicants' have failed to address DNA. Southern blots allow hybridization of DNA, but not by the instantly claimed methods. Thus, in view of the instant claim language drawn to hybridization procedures using only RNA, there is no disclosure of RNA techniques using DNA. Therefore applicants' arguments are not persuasive.

Applicants' assert that the examiner is wrong with respect to a primer being a nucleic acid which hybridizes to a target. However it is the examiner's position that a primer is a nucleic acid necessary to initiate replication and requires the presence of the 5' end of the chain being synthesized in a stable base paired complex. Applicants' have failed to disclose the identity of the nucleic acid sequence which will initiate replication. Applicants' have pointed to claim language and a definition yet still have failed to disclose the nucleic acid identity of the primer. Therefore, applicants' assertion that the examiner's position is incorrect is not persuasive. Especially when applicants' have failed to disclose a method for determining gene expression solely by hybridization. Applicants' have failed to correlate determining the presence of a gene with a method for determining gene expression. Applicants' have failed to disclose within the specification how a person would determine whether a gene is expressed simply by determining hybridization. Therefore the rejection is maintained for the reasons stated above.

The new matter rejection of claims 51-58 and 60-61 are rejected under 35 U.S.C. 112, first paragraph, is maintained for reasons already of record. Applicants' assert that the examiner does not accept that the described method will de facto determine expression. However, the issue is not whether the examiner accepts the statement, the issue is whether there is support for the claims in the specification. As stated above, applicants' support is drawn only to hybridization, PCR and blotting techniques. There is no support for simply using hybridization to determine protein expression. There are no experiments that teach that if a nucleic sequence hybridizes, one can determine expression of a gene which encodes a human polypeptide that has PI3 kinase activity by the claimed steps. It is also noted that attorney's assertions to the contrary without support from the instant specification are not adequate to provide support for the new matter. Applicants' have still failed to show support for such a method. Applicants have only shown support hybridization techniques. Therefore the rejection will be maintained.

The rejection of claims 51-58 and 60-61 under 35 U.S.C. 112, second paragraph, is maintained. Applicants' only argument is that hybridization de facto equates to expression of the gene. However, as stated above, the conclusion that hybridization de facto equates to gene expression is not supported by the claims or specification. And the mere presentation of applicants' statements are not persuasive, in view of the lack of scientific evidence. The stringency conditions do not teach the essential elements necessary to determine gene expression from hybridization. Thus the claims fail to teach how once the annealing process de facto equates to the determination of gene expression. Applicants' have failed to point to support in the specification or claims which positively recite the active steps necessary to determine gene expression. There is no step for the amplification of the hybridized nucleic acid molecule by PCR, there is no step for the expression of the product, no immunoprecipitation step, there is no step which determines whether the cDNA encoded a polypeptide with a molecular weight of 110 that possesses PI-3 kinase activity. Finally, there is no step which correlates the determination of hybridization to the determination of expression or the presence of said gene. Thus, applicants' arguments are not persuasive and the rejections are maintained.